PATENT COOPERATION TREATY

2026-4303PC
Muller

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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CASE 2026-4303PC ATTY KAM
DUE September 28 2001 (Written opinion)
1 mo. call-up August 28 2001
BY J. M.

PCT

WRITTEN OPINION

(PCT Rule 66)

Date of mailing *(day/month/year)*	28.06.2001
Applicant's or agent's file reference: 2026-4303PC	**REPLY DUE** **within 3 month(s)** from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/15527	02/06/2000	04/06/1999

International Patent Classification (IPC) or both national classification and IPC
C12N15/86

Applicant
NATIONAL INSITUTES OF HEALTH

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☐	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☒	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain document cited
VII	☐	Certain defects in the international application
VIII	☐	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4. For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis. For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 04/10/2001.

Name and mailing address of the international preliminary examining authority:
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Authorized officer / Examiner
Paresce, D

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I. Basis of the opinion

1. With regard to the **elements** of the international application (Replacement *sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed"*):

Description, pages:

1-37 as originally filed

Claims, No.:

1-21 as originally filed

Drawings, sheets:

1/19-19/19 as originally filed

Sequence listing part of the description, pages:

1-36, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:
   ☐ the claims, Nos.:
   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation (Form PCT/IPEA/405) to restrict or pay additional fees, the applicant has:

   ☐ restricted the claims.

   ☒ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with for the following reasons and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees:

3. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this opinion:

   ☒ all parts.

   ☐ the parts relating to claims Nos. .

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	11-13
Inventive step (IS)	Claims	
Industrial applicability (IA)	Claims	

2. Citations and explanations
   see separate sheet

Lack of unity (Rule 13.1 PCT):

The documents mentioned in this communication are numbered as in the search report, i.e. D1 corresponds to the first document of the search report.

The IPEA agrees with the objection put forward by the Search Division as to lack of unity (Rule 13.1 PCT). The IPEA is also of the opinion that the present set of claims relates to two different inventions (see International Search Report). The separate inventions/groups of invention are:

1) Claims 1-6, 11-13 (completely) and 9-10, 14-21 (partially) are directed to a nucleic acid molecule comprising a chimeric virus genome, said genome being a BVDV genome in which the structural region of the BVDV genome has been replaced by the structural region of a hepatitis C virus genome. The claims are further directed to a DNA construct comprising said molecule, an RNA transcript of said DNA construct, a host cell transfected with said DNA construct or RNA construct, a chimeric HCV-BVDV produced by said host cell and a composition comprising said virus.

2) Claims 7-8 (completely) and 9-10, 14-21 (partially) are directed to a nucleic acid molecule comprising a chimeric virus genome, said genome being a BVDV genome in which the non-structural region of the BVDV genome has been replaced by the non-structural region of a hepatitis C virus genome. The claims are further directed to a DNA construct comprising said molecule, an RNA transcript of said DNA construct, a host cell transfected with said DNA construct or RNA construct, a chimeric HCV-BVDV produced by said host cell and a composition comprising said virus.

The general inventive concept underlying the two above identified inventions of the present application can be seen as the provision of chimeric BVDV-hepatitis C virus genomes. This general inventive concept, however, is not considered novel because, as illustrated by D1, the concept of providing chimeric BVDV-hepatitis C virus genomes was known in the prior art. In D1, a functional clone of BVDV was used to construct and characterize a series of 5' NTR chimeras with sequences derived from the hepatitis C virus (HCV) as well as other flaviviruses. The results

of this study help to define the requirements of a functional BVDV 5' NTR and provide replication-competent BVDV-HCV chimeras dependent on a functional HCV internal ribosome entry site (see D1, p. 1419).

In view of D1, the problem underlying the present application is considered as the provision of further BVDV-HCV chimeric genomes. One solution to this problem provides a chimeric virus genome, said genome being a BVDV genome in which the structural region of the BVDV genome has been replaced by the structural region of a hepatitis C virus genome. The second solution is considered the provision of a chimeric virus genome, said genome being a BVDV genome in which the non-structural region of the BVDV genome has been replaced by the non-structural region of a hepatitis C virus genome.

In response to an invitation to pay additional fees (see Form PCT/IPEA/405), the Applicant paid the additional examination fees. Consequently the international preliminary examination will be based on claims 1-21 of the present application.

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1) Novelty: Article 33(2) PCT

D1 discloses the construction and characterization of a series of BVDV-hepatitis C virus (HCV) 5' NTR chimeras. The results of this study help to define the requirements of a functional BVDV 5' NTR and provide replication-competent BVDV-HCV chimeras dependent on a functional HCV internal ribosome entry site (see D1, p. 1419).

D2 discloses chimeric genomes of poliovirus in which the cognate internal ribosomal entry site element was replaced by genetic elements of hepatitis C virus (see abstract).

D3 presents a review of flavivirus research and, in particular, flavivirus vaccines. D3 mentions the development of chimaeric viruses as potential vaccine

candidates. D3 discloses dengue virus chimeras, TBE/dengue virus chimeras, poliovirus expression vectors and mentions developments in generating RNA viruses from cloned cDNA (see p. 975).

D4 and D5 describe the sequence and structural elements of BVDV (see abstracts).

The subject-matter of claims 11-13 is not considered new in the sense of Article 33(2) PCT for the following reasons: The subject-matter of these claims, when interpreted in the broadest sense possible, covers any polypeptide encoded by a BVDV nucleic acid sequence or a hepatitis C virus nucleic acid sequence. BVDV and hepatitis C virus proteins were known in the prior art at the priority date of the present application (see D1-D5). Therefore, these claims are not considered novel.

VI: Certain documents cited

Certain published documents (Rule 70.10)

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO9955366	04.11.99	23.04.99	24.04.98

1) Additional comments:

Should the applicant file a new set of claims, which take account of the above comments, he is requested to clearly identify the amendments carried out, no matter whether they concern amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based (see Rule 66.8(a) PCT), to facilitate the examination of the conformity of the amended application with the requirements of Article 34(2)(b) PCT. If the applicant regards it as appropriate these indications could be submitted in handwritten form on a copy of the relevant parts of the application as filed. The attention of the Applicant is drawn to the fact that the application may not be amended in such a way that it contains subject-matter which extends beyond the content of the application as filed, Article 34(2)(b) PCT.